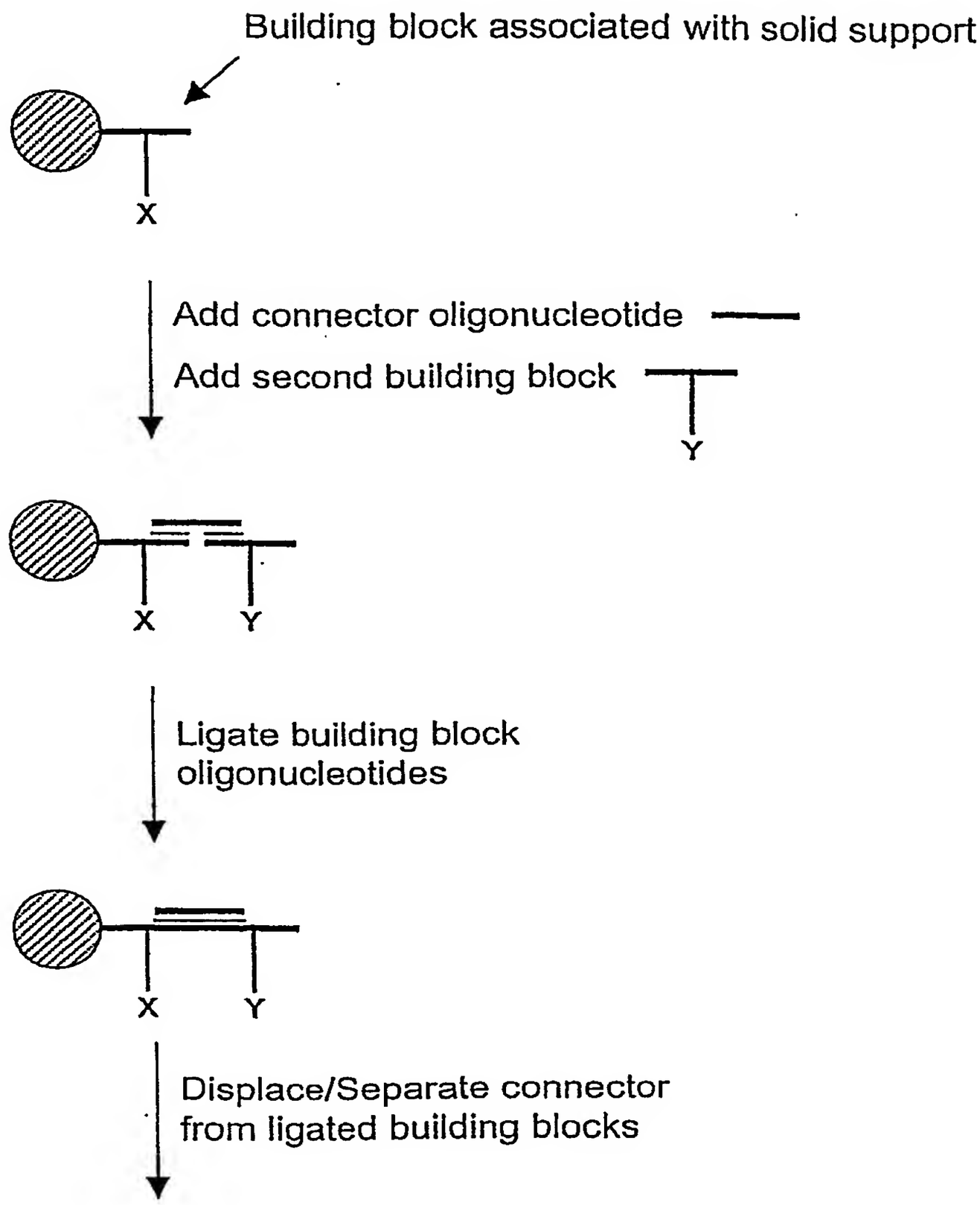
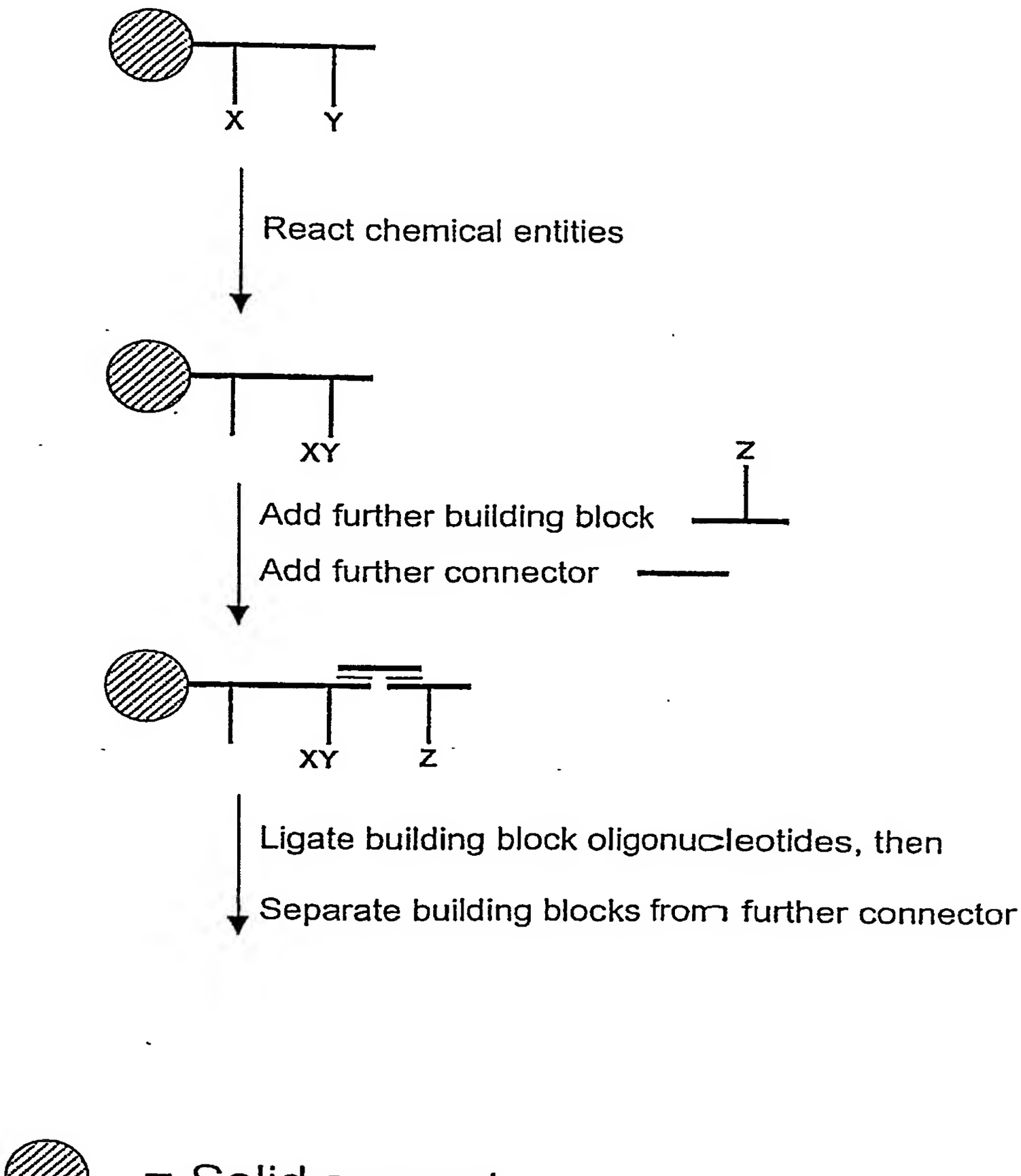
Figure 1A



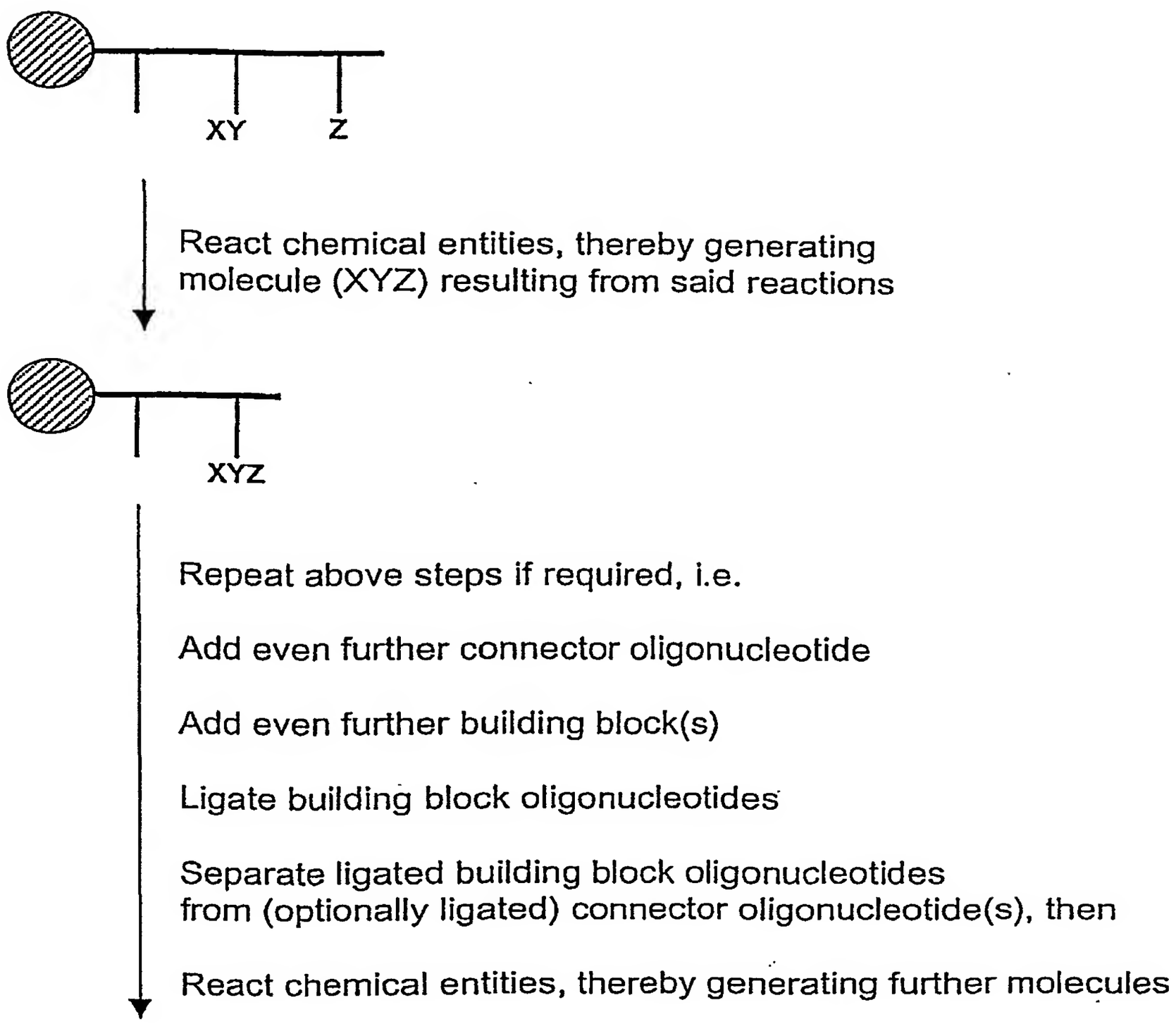
= Solid support

Figure 1B



= Solid support

Figure 1C



= Solid support

Figure 2A

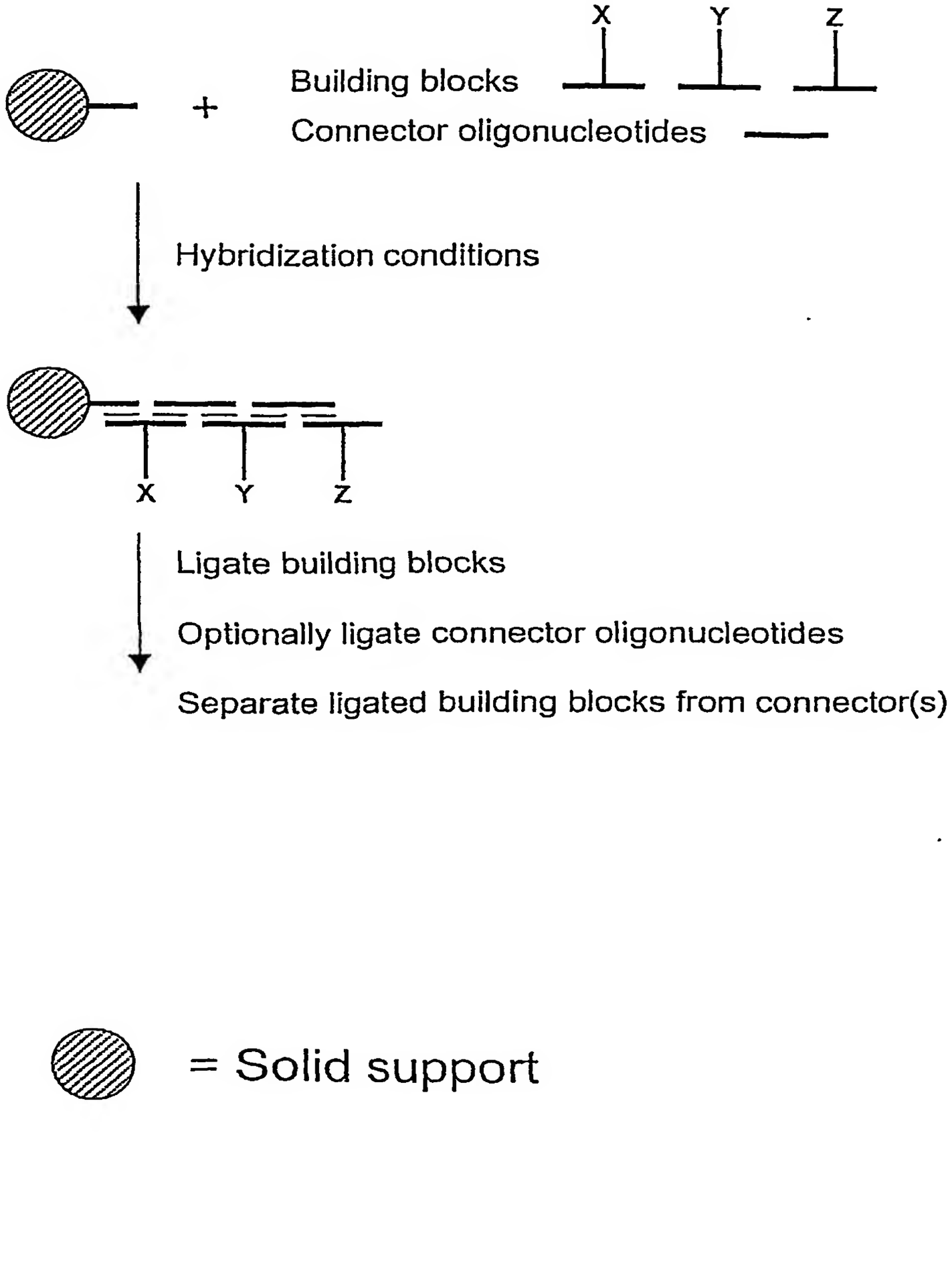
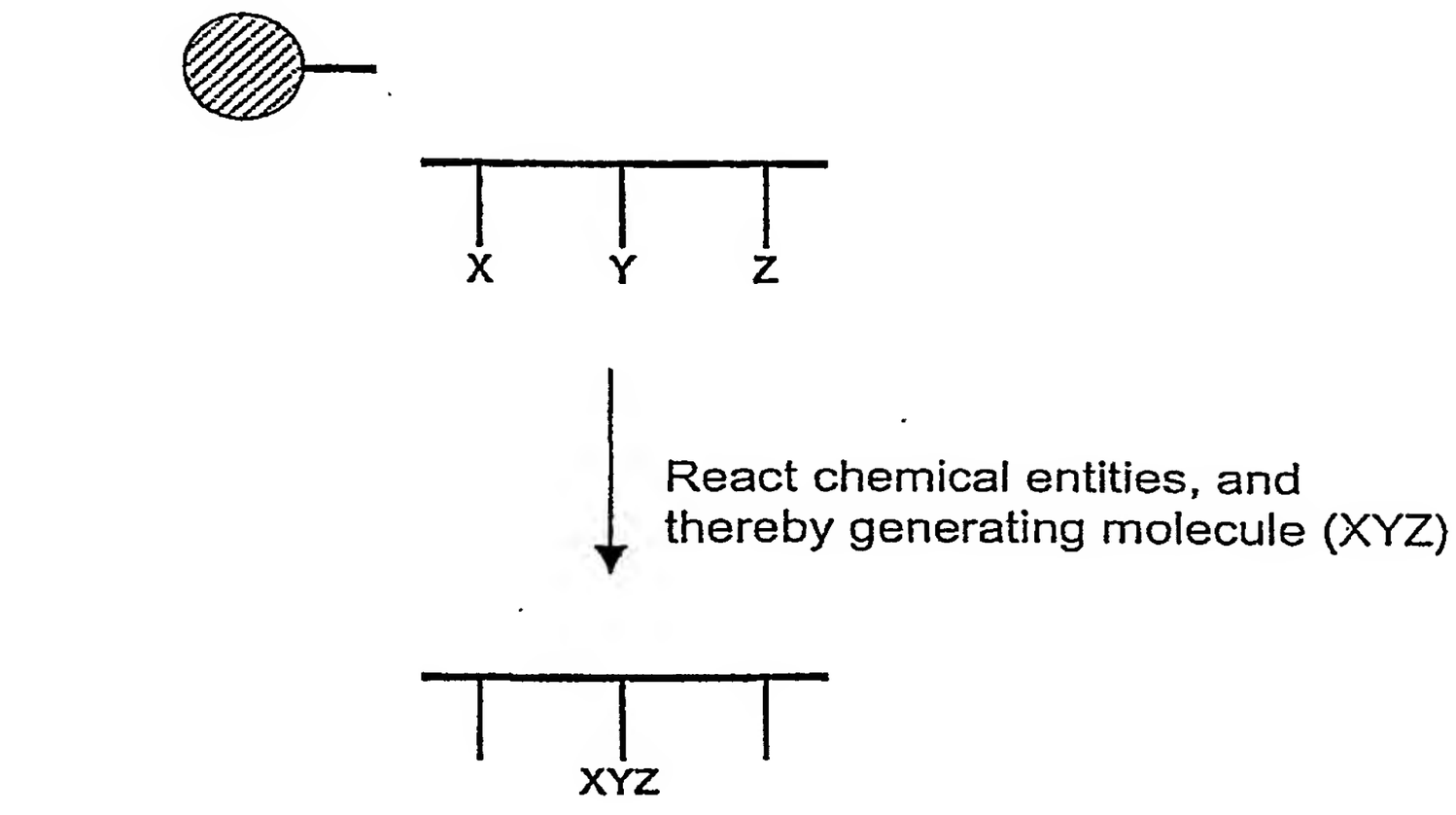

X
Y
Z
Building blocks
+
Connector oligonucleotides
Hybridization conditions
X
Y
Z
Ligate building blocks
Optionally ligate connector oligonucleotides
Separate ligated building blocks from connector(s)
= Solid support

Figure 2B



= Solid support

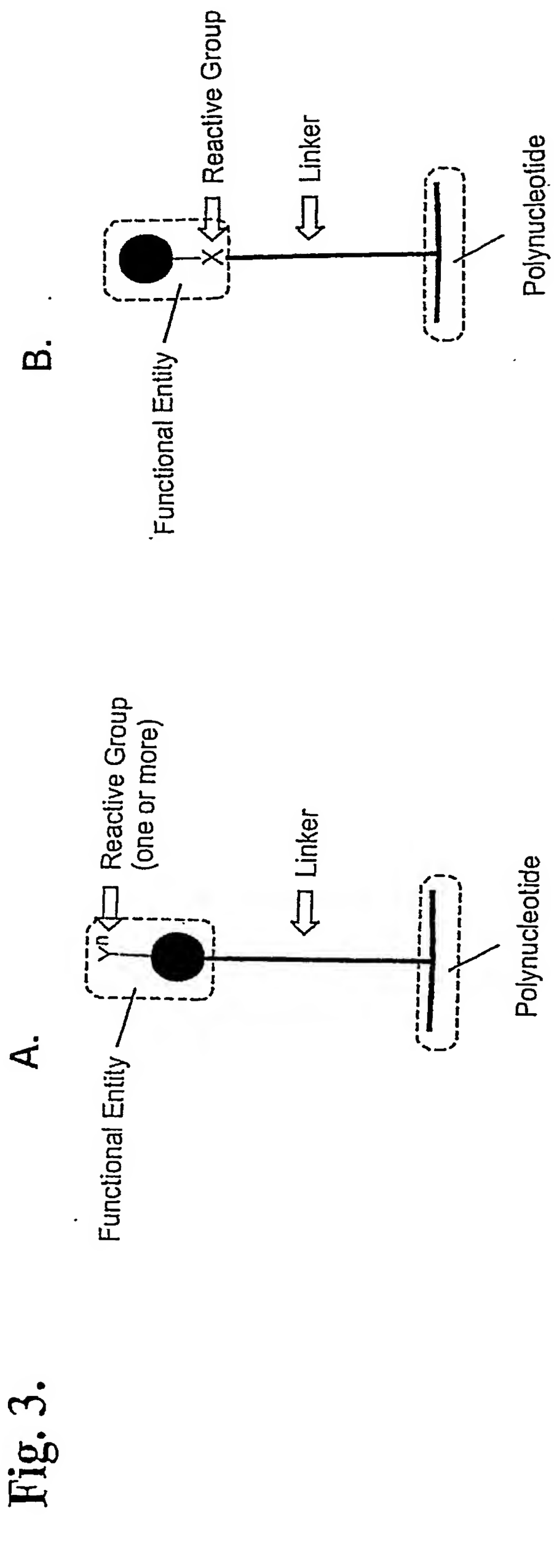

A.
Functional Entity
Reactive Group (one or more)
Linker
Polynucleotide
B.
Entity
X
Reactive Group
Linker
Polynucleotide
C.
Functional Entity
Reactive Group (one or more)
X
Reactive Group
Linker
Polynucleotide
D.
Reactive Group (one or more)
Linker
Polynucleotide
E.
Polynucleotide

Fig. 3.

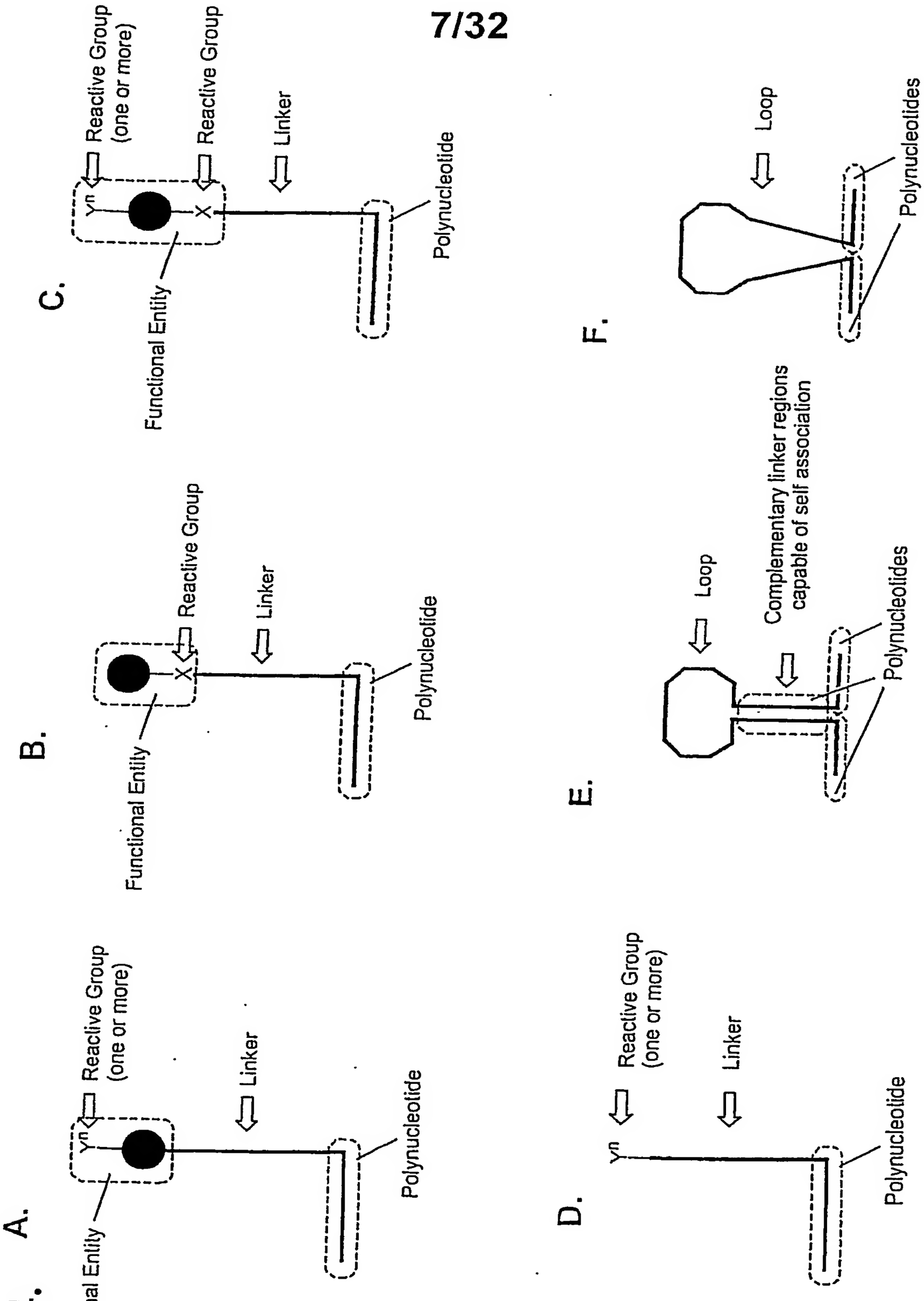

A.
Reactive Group (one or more)
Yn
Functional Entity
Linker
Polynucleotide
B.
Functional Entity
X
Reactive Group
Linker
Polynucleotide
C.
Reactive Group (one or more)
Yn
X
Functional Entity
Linker
Polynucleotide
D.
Reactive Group (one or more)
Yn
Linker
Polynucleotide
E.
Loop
Complementary linker regions capable of self association
Polynucleotides
F.
Loop
Polynucleotides

Fig. 4.

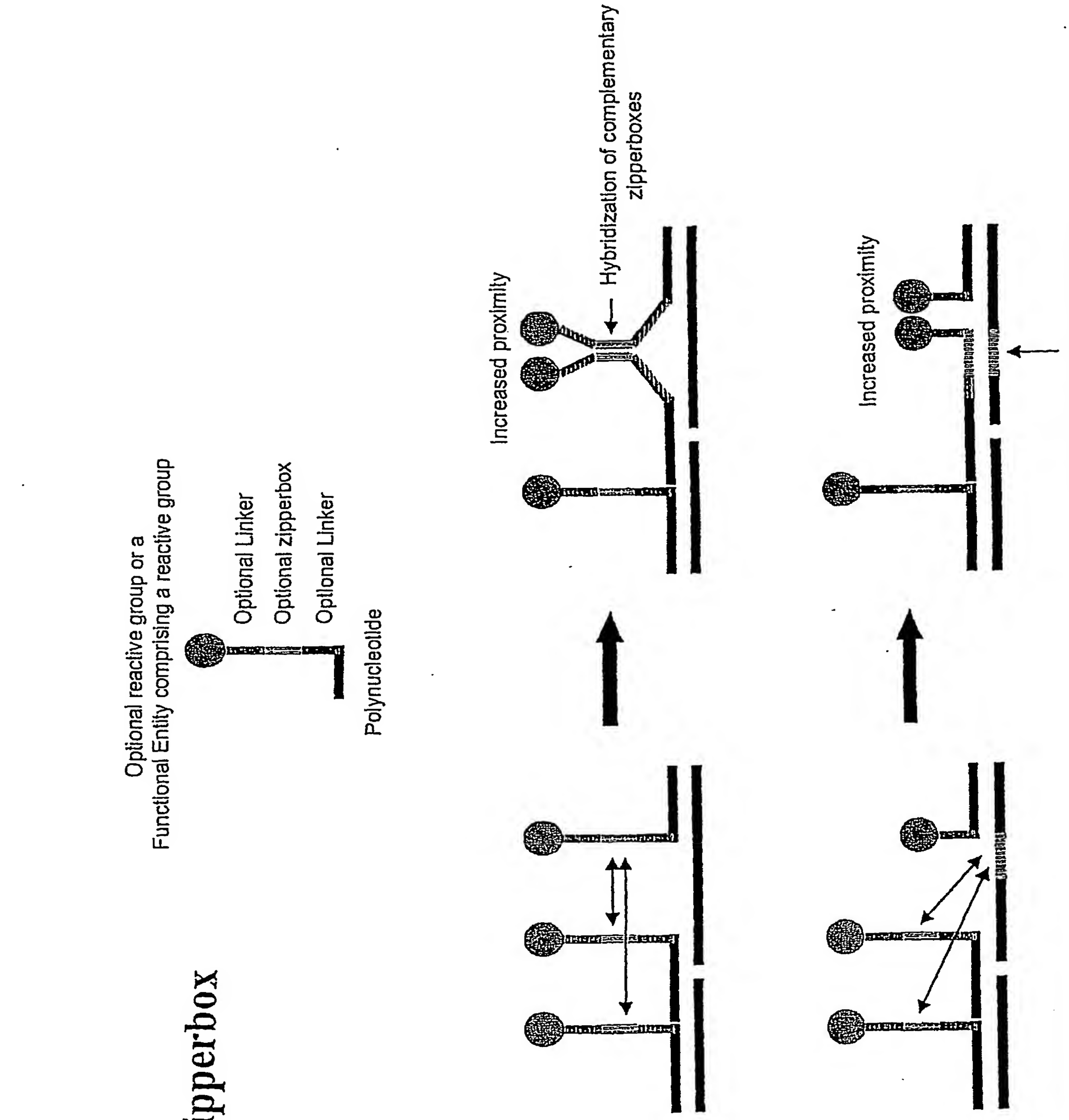
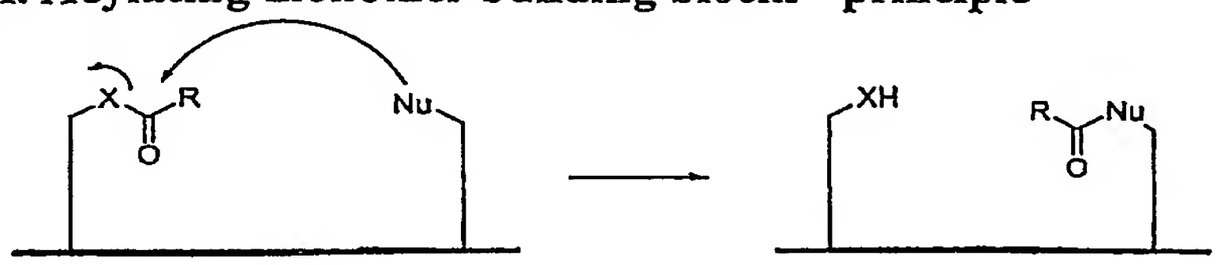


Fig. 5. Zipperbox

Fig. 6. Reaction types allowing simultaneous reaction and linker cleavage.

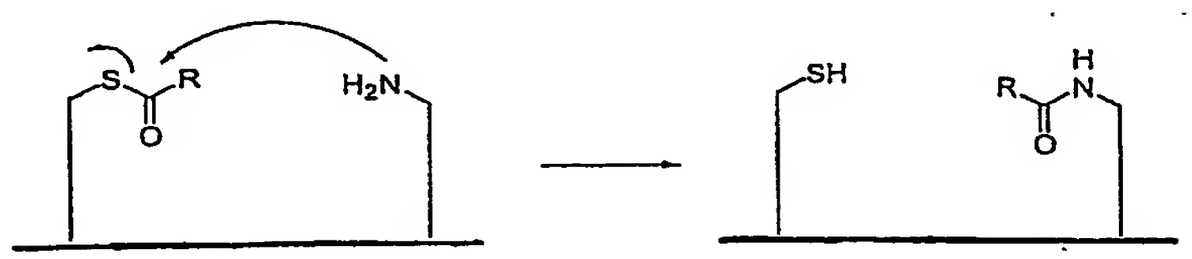
Nucleophilic substitution using activation of electrophiles

A. Acylating monomer building blocks - principle

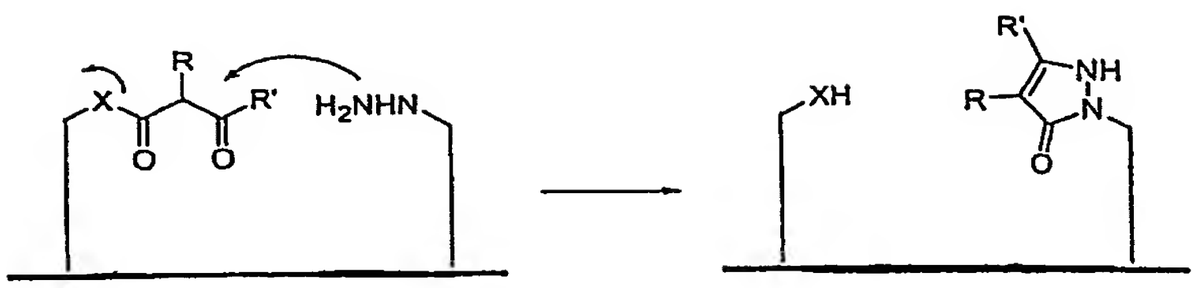


X = O, S Nu = Oxygen- , Nitrogen- , Sulfur- and Carbon Nucleophiles

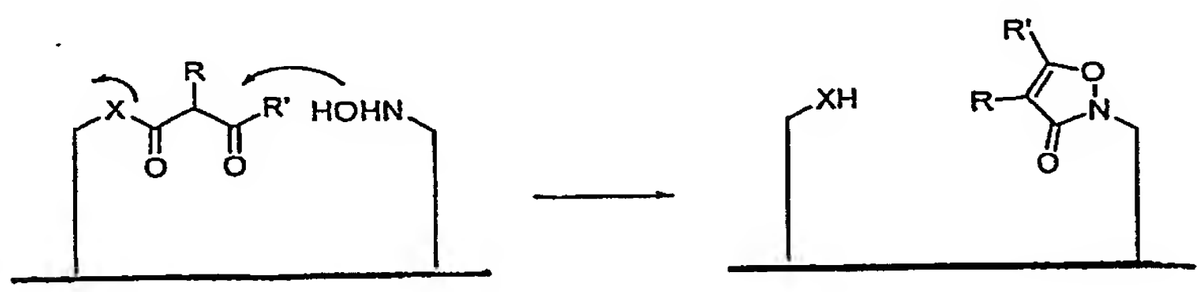
B. Acylation
Amide formation by reaction of amines with activated esters



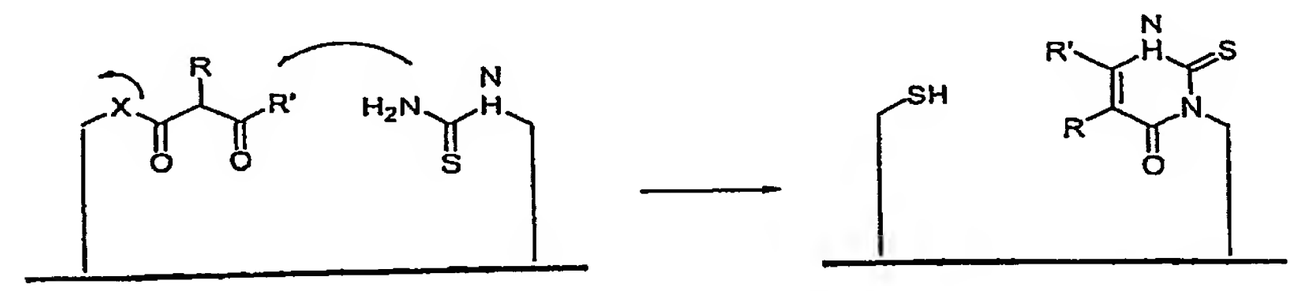
C. Acylation
Pyrazolone formation by reaction of hydrazines with β–Ketoesters



D. Acylation
Isoxazolone formation by reaction of hydroxylamines with β–Ketoesters

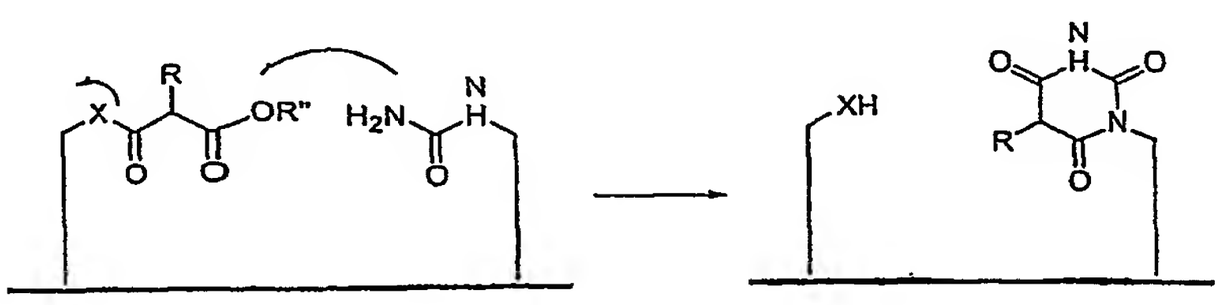


E. Acylation
Pyrimidine formation by reaction of thioureas with β–Ketoesters

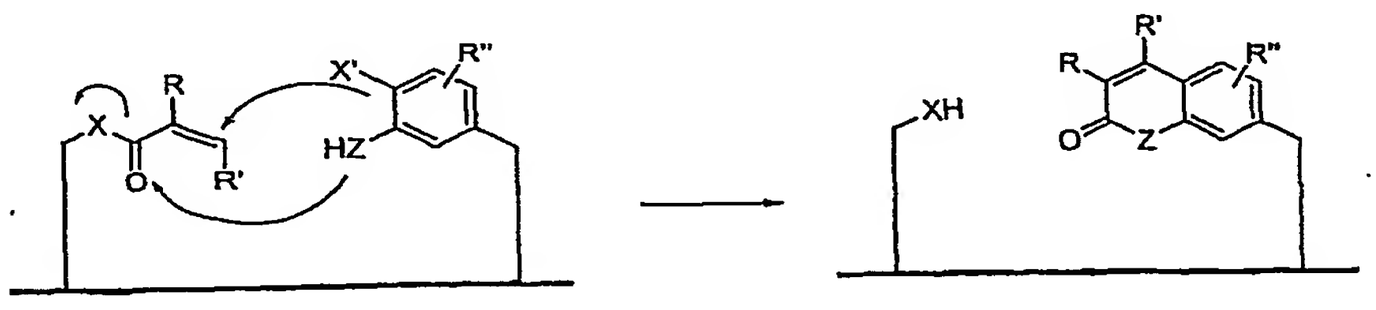


F. Acylation

Pyrimidine formation by reaction of ureas with Malonates

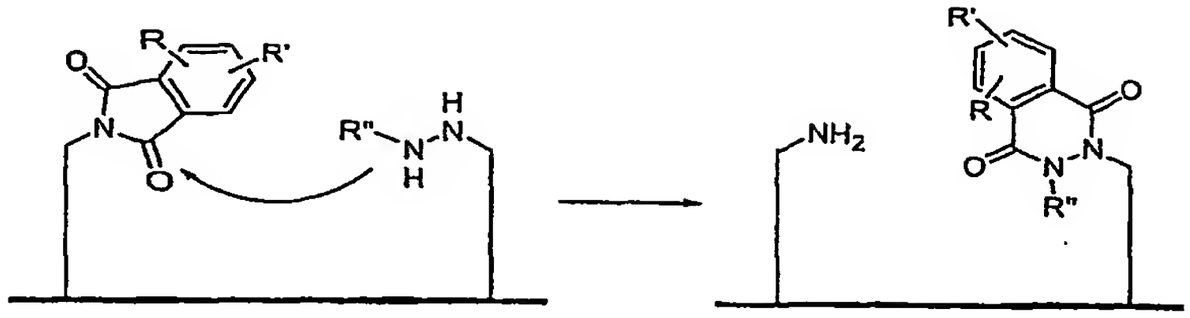


G. Acylation
Coumarine or quinolinon formation by a Heck reaction followed by a nucleophilic substitution

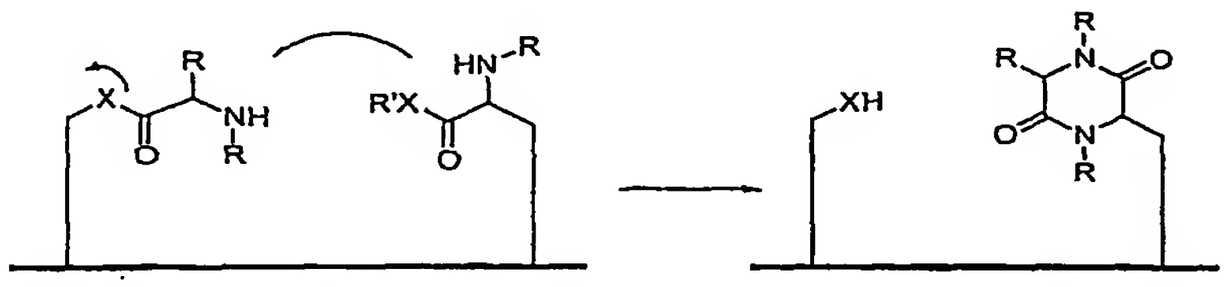


X = O,S X' = Halogen, OTf, OMs Z = O, NH

H. Acylation
Phthalhydrazide formation by reaction of Hydrazines and Phthalimides

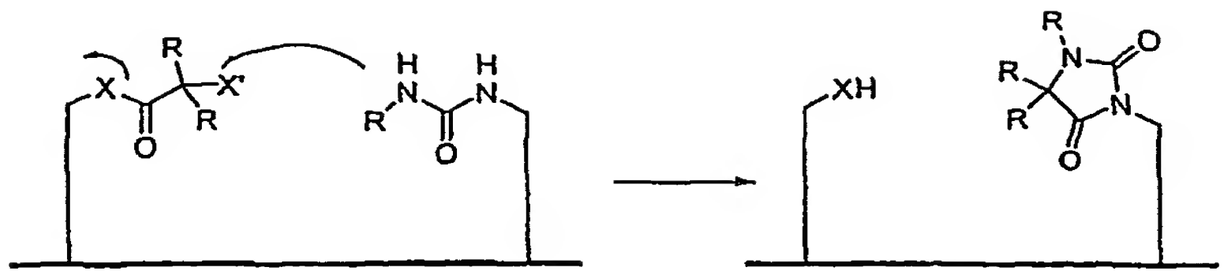


I. Acylation
Diketopiperazine formation by reaction of Amino Acid Esters



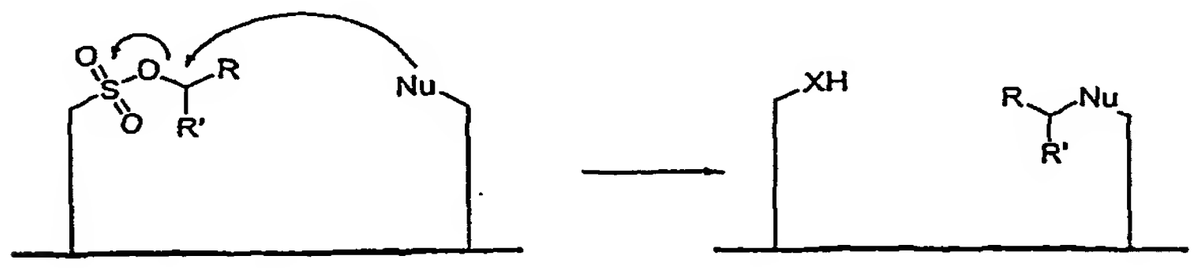
X = O, S R' = H, R

J. Acylation
Hydantoin formation by reaction of Urea and α-substituted Esters



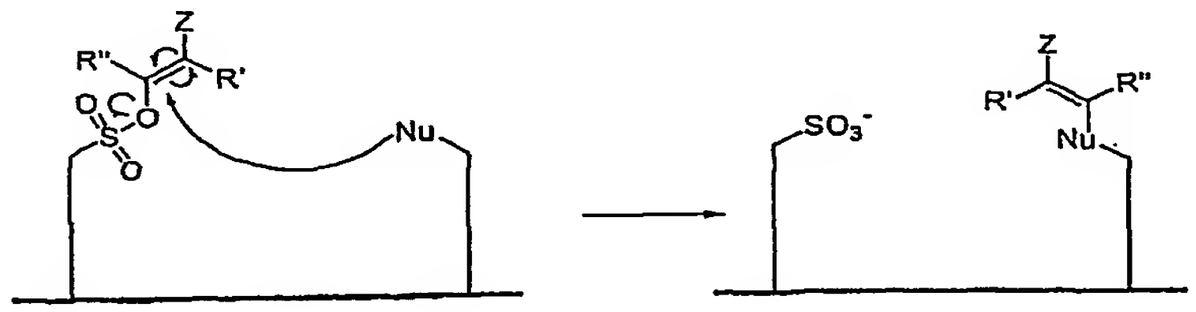
X = O, S X' = Hal, OTos, OMs, etc.

K. Alkylating monomer building blocks - principle
Alkylated compounds by reaction of Sulfonates with Nucleofiles



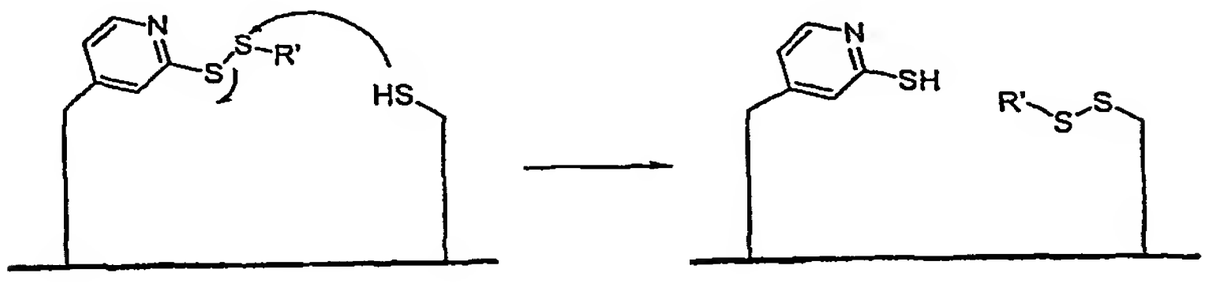
Nu = Oxygen- , Nitrogen- , Sulfur- and Carbon Nucleophiles

L. Vinylating monomer building blocks - principle

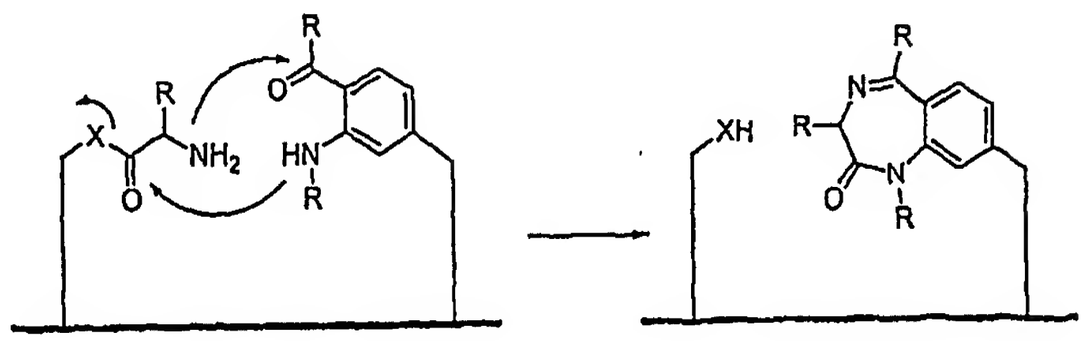


Z = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F
Nu = Oxygen- , Nitrogen- , Sulfur- and Carbon Nucleophiles

M. Heteroatom electrophiles
Disulfide formation by reaction of Pyridyl disulfide with mercaptanes



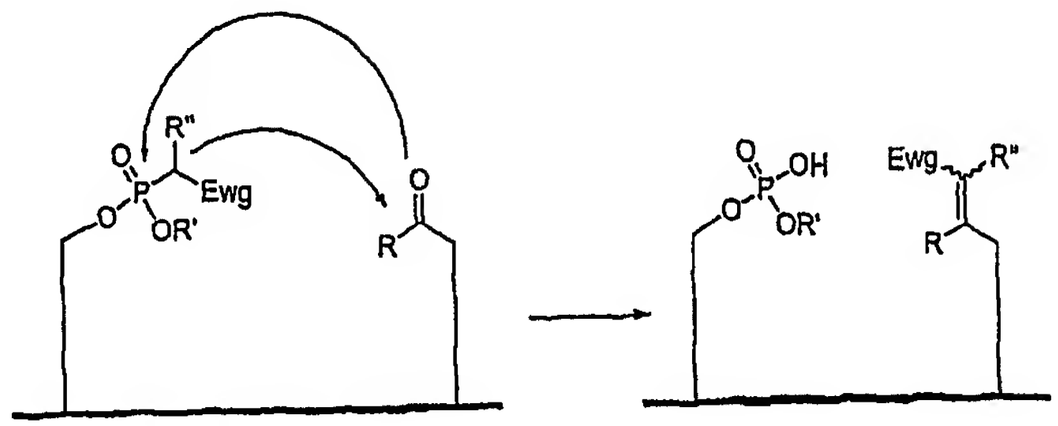
N. Acylation
Benzodiazepinone formation by reaction of Amino Acid Esters and Amino Ketones



X = O, S

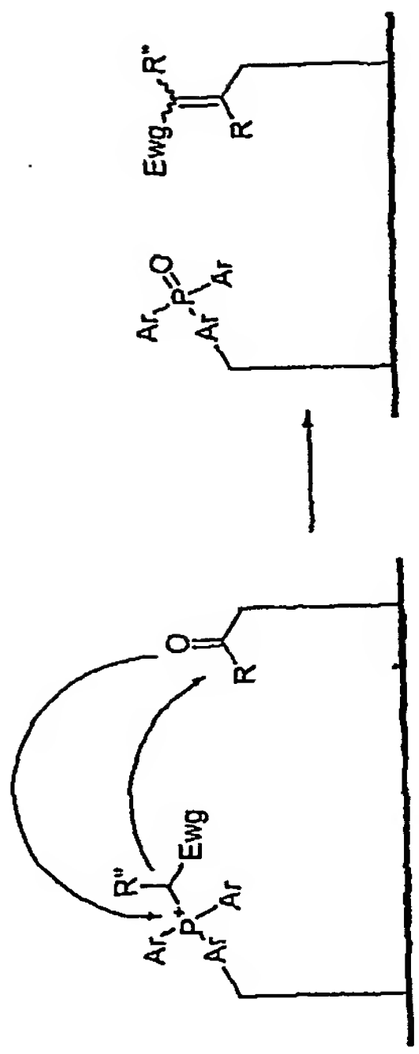
Addition to carbon-hetero multiple bonds

O. Wittig/Horner-Wittig-Emmons reagents
Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones



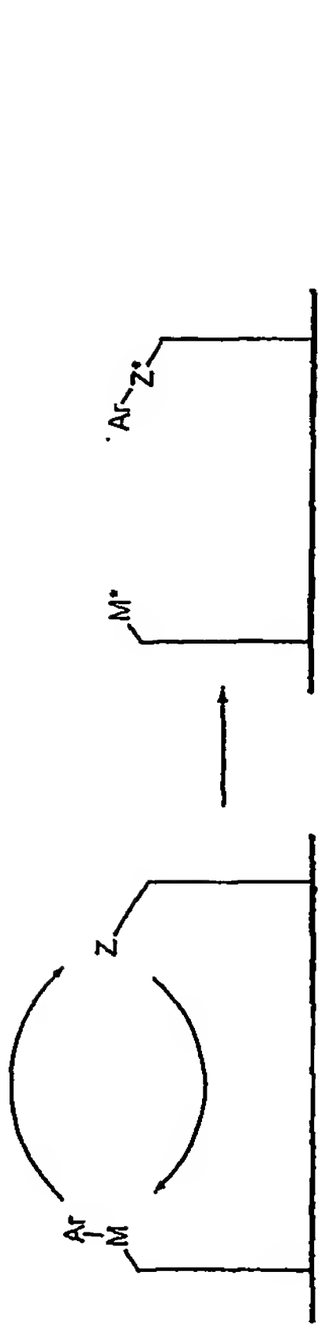
Ewg = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F etc.

P. Wittig/Horner-Wittig-Emmons reagents
Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones



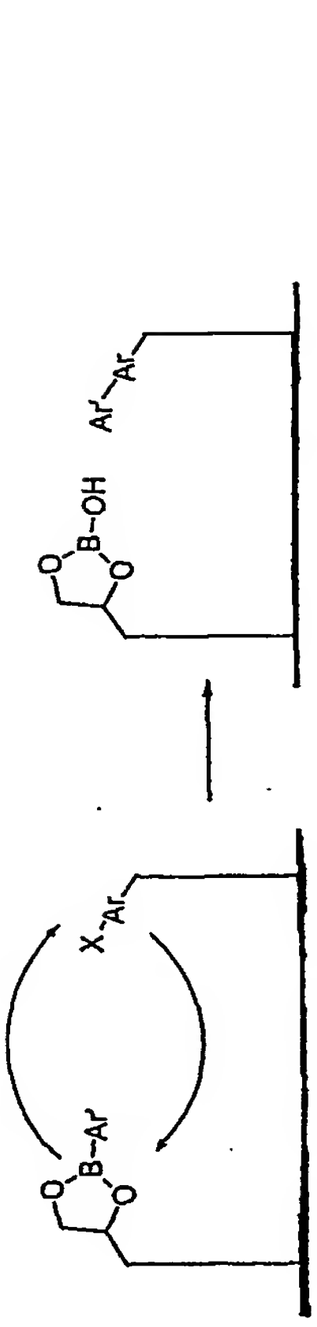
Transition metal catalysed reactions

Q. Transition metal cat. Arylations



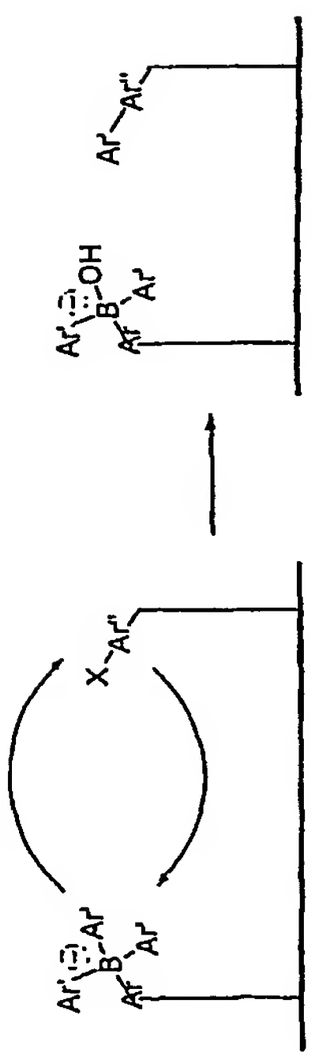
Z = haloaryl, halohetaryl, ArOMs, ArOTf, ArOTos or NHR or OH or SH etc.
Z* = Aryl, hetaryl, NR or O or S etc
M = e.g. BR, BR_2^-, SnR_2 etc.
R = H, alkyl, aryl, hetaryl, OR, NR_2
M* = e.g. $B(OH)R$, $B(OH)R_2^-$, $Sn(OH)R_2$ etc.

R. Arylation
Biaryl formation by the reaction of Borates with Aryls or Heteroaryls

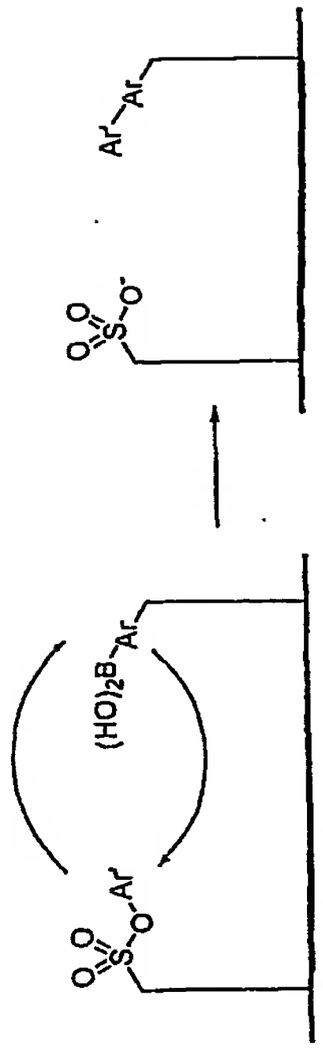


X = Halogen, OMs, OTf, OTos, etc

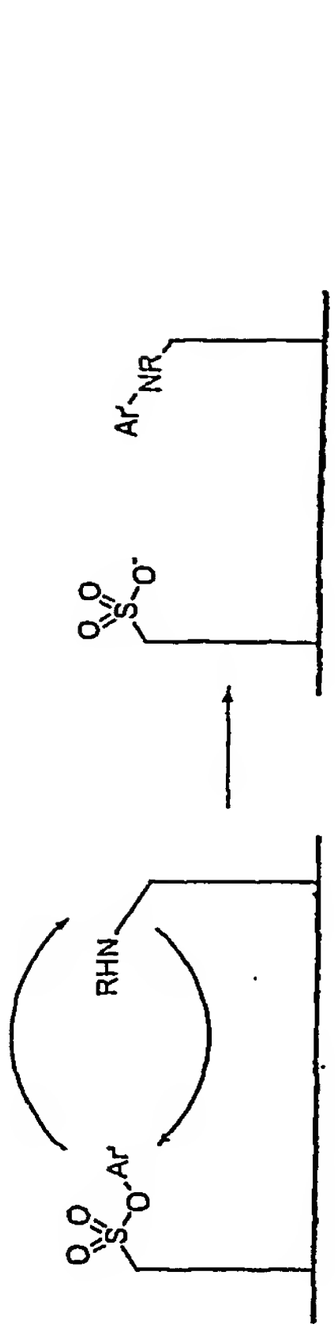
S. Arylation
Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls



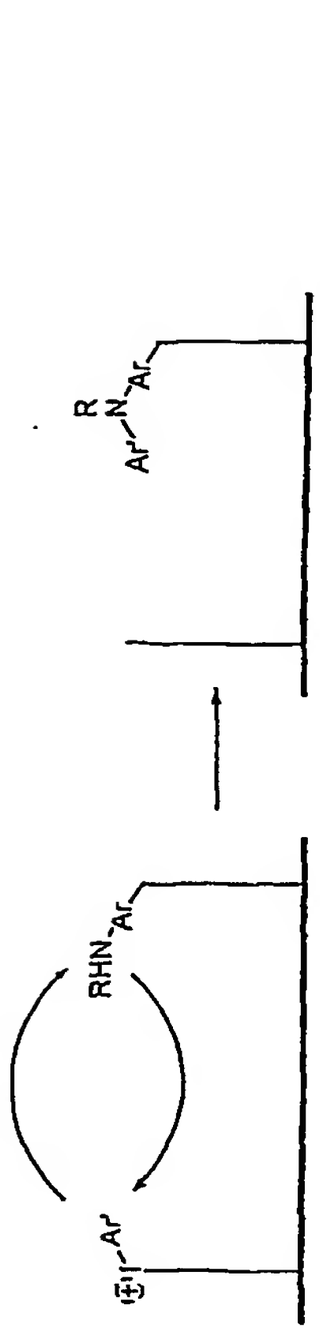
T. Arylation
Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls



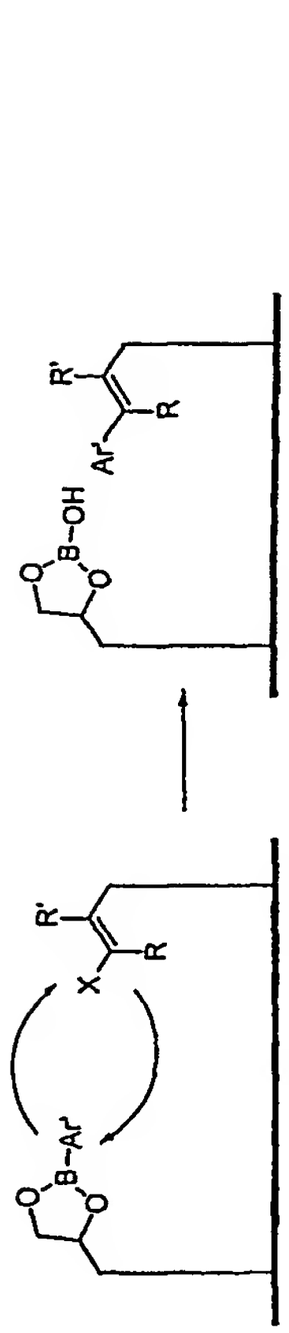
U. Arylation
Arylamine formation by the reaction of amines with activated Aryls or Heteroaryls



V. Arylation
Arylamine formation by the reaction of amines with hypervalent iodonium salts

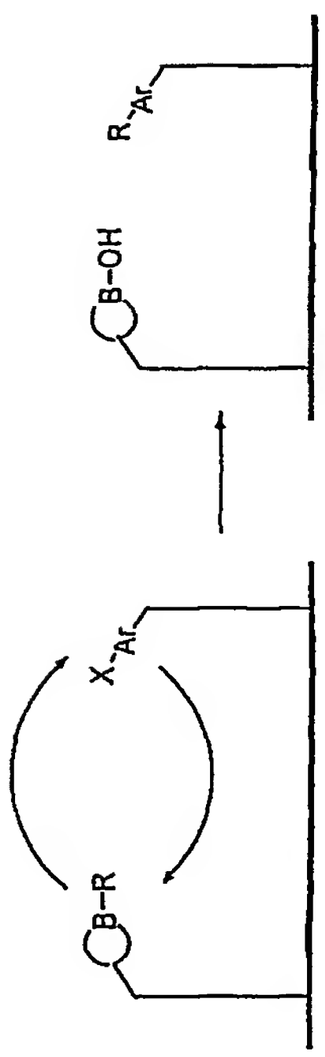


X. Arylation
Vinylarene formation by the reaction of alkenes with Aryls or Heteroaryls



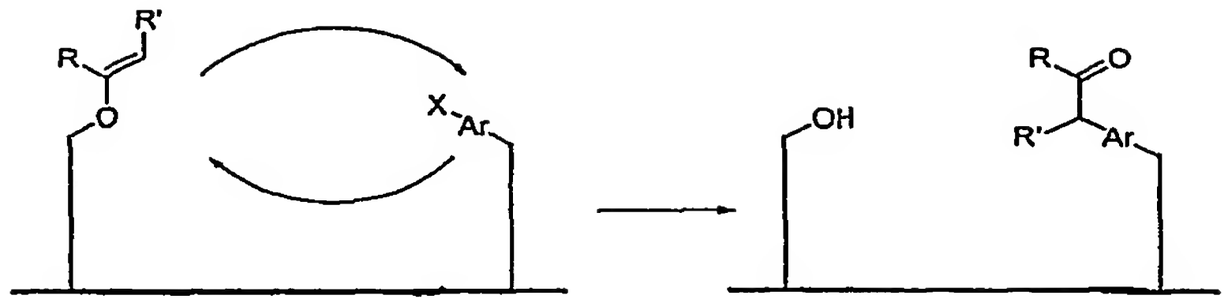
X = Halogen, OMs, OTf, OTos, etc

Y. Alkylation
Alkylation of arenes/hetarens by the reaction with Alkyl boronates



X = Halogen, OMs, OTf, OTos, etc

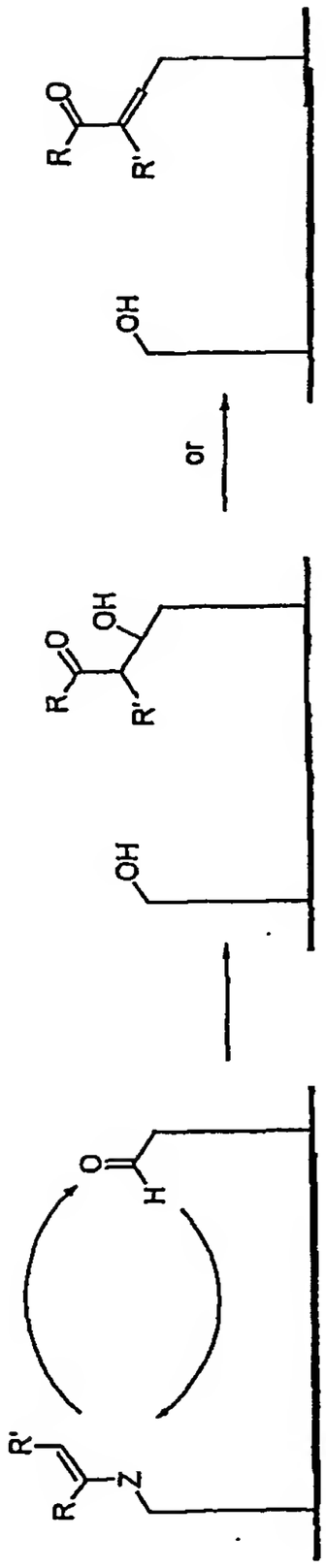
Z. Alkylation
Alkylation of arenes/hetarenes by reaction with enolethers



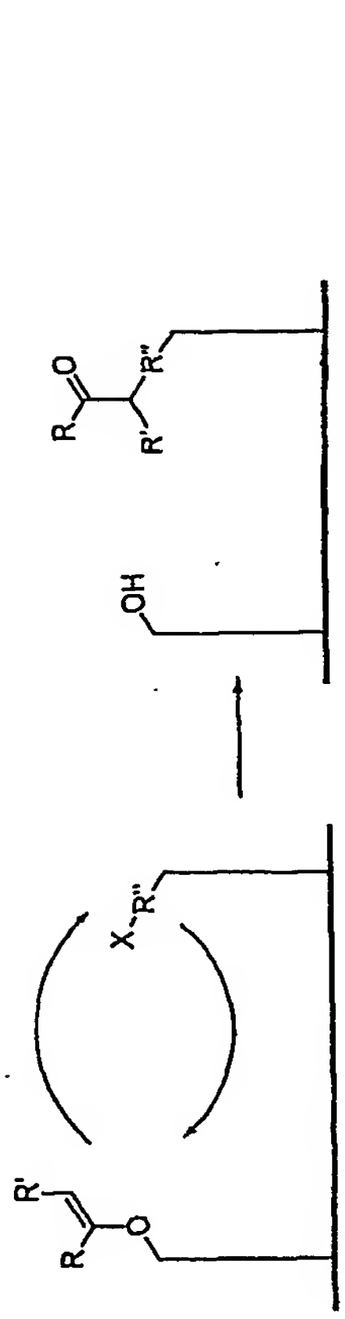
X = Halogen, OMs, OTf, OTos, etc

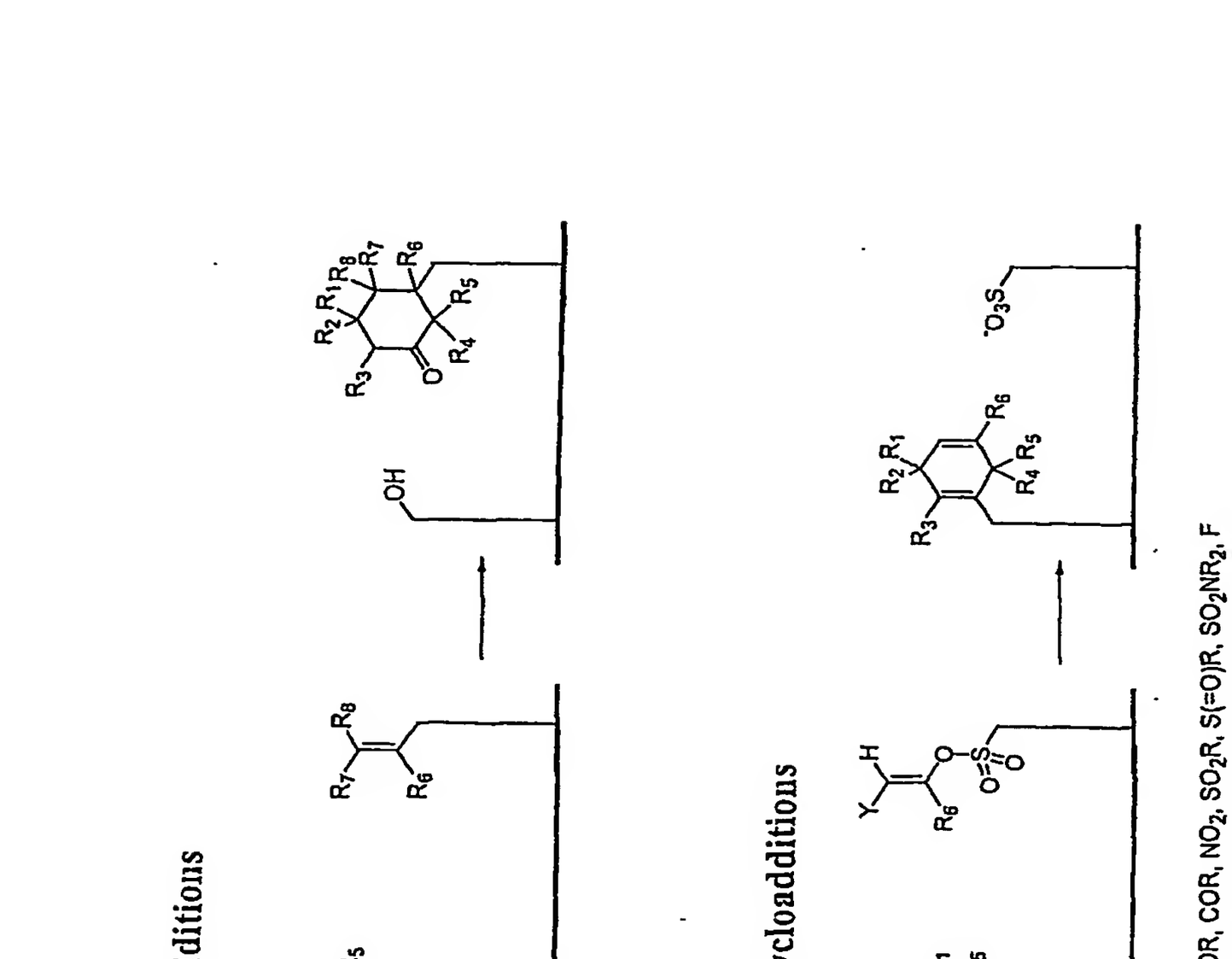
Nucleophilic substitution using activation of nucleophiles

AA. Condensations
Alkylation of aldehydes with enolethers or enamines

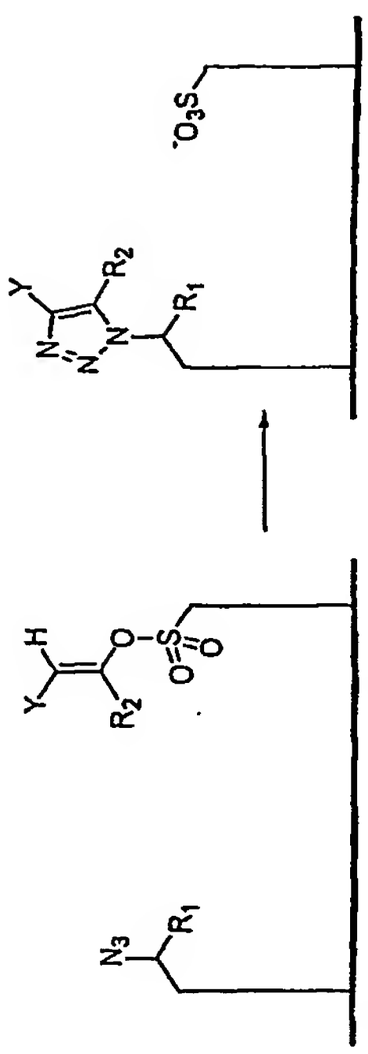


AB. Alkylation
Alkylation of aliphatic halides or tosylates with enolethers or enamines



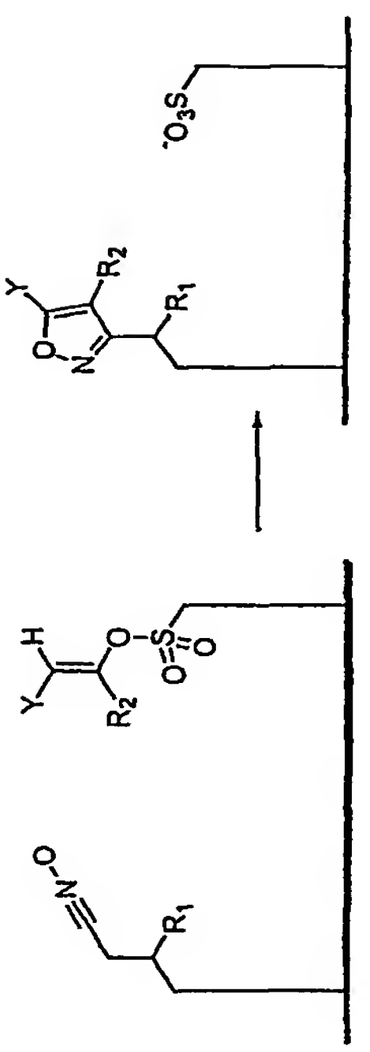

Cycloadditions
AC. [2+4] Cycloadditions
OH
Z = O, NR
AD. [2+4] Cycloadditions
Y = CN, COOR, COR, NO2, SO2R, S(=O)R, SO2NR2, F

AE. [3+2] Cycloadditions



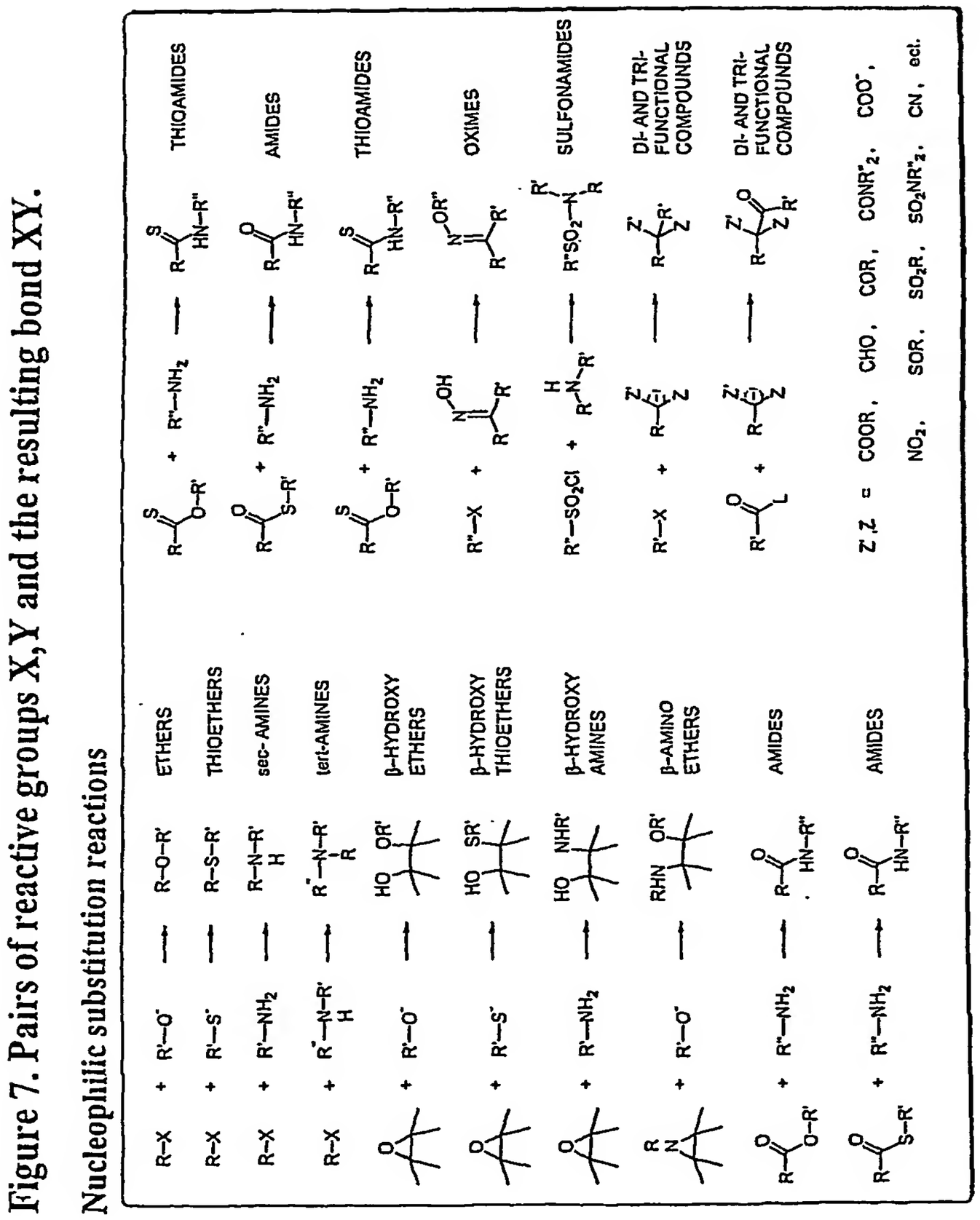
Y = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F

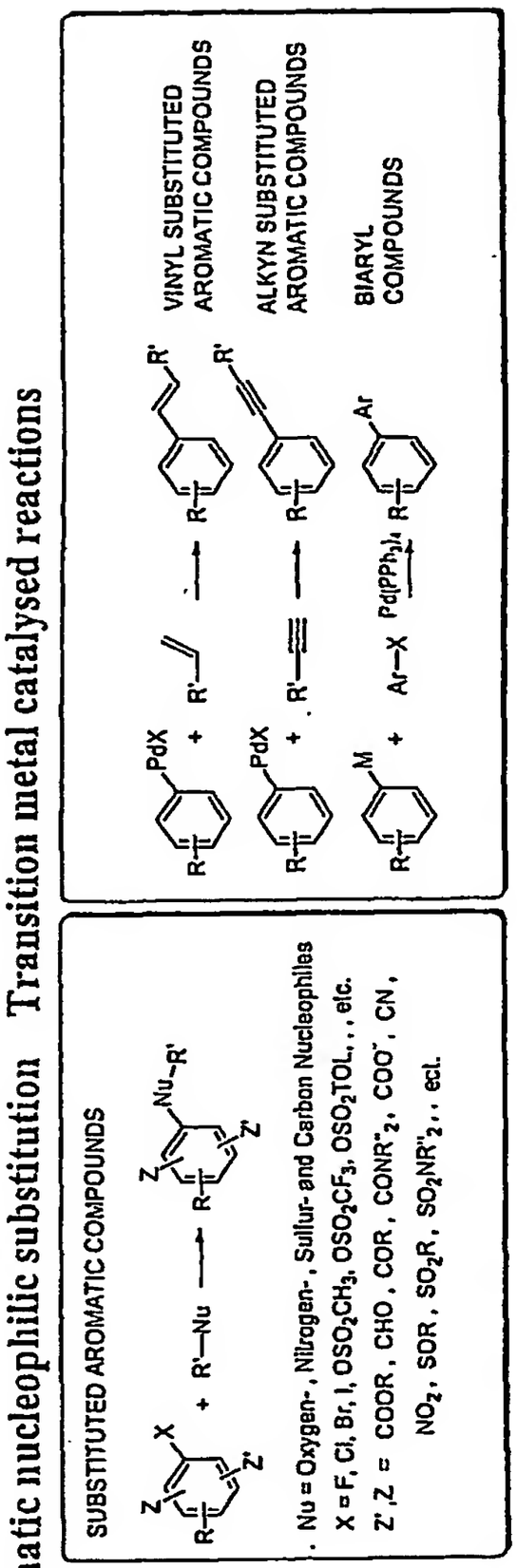
AF. [3+2] Cycloadditions

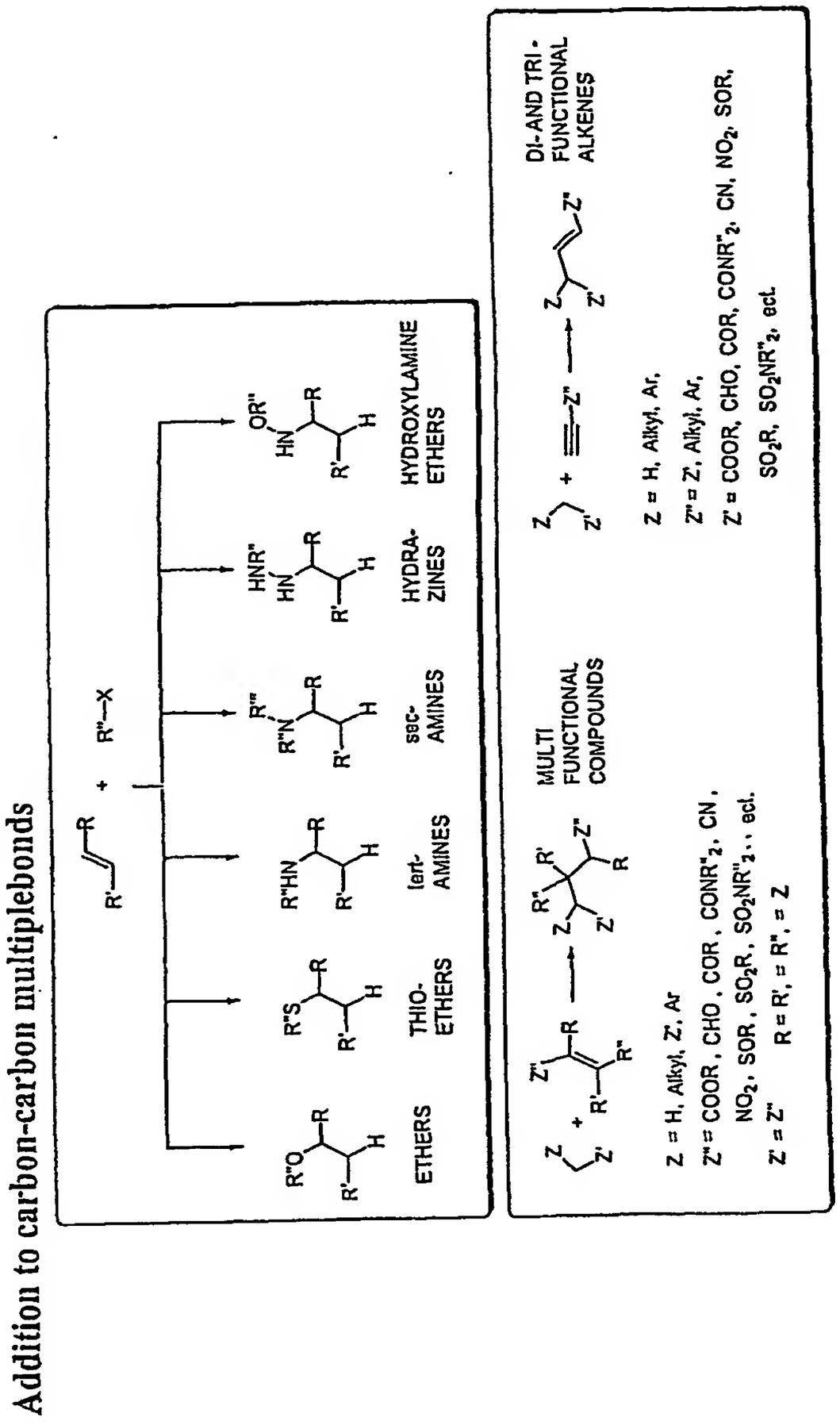


Y = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F

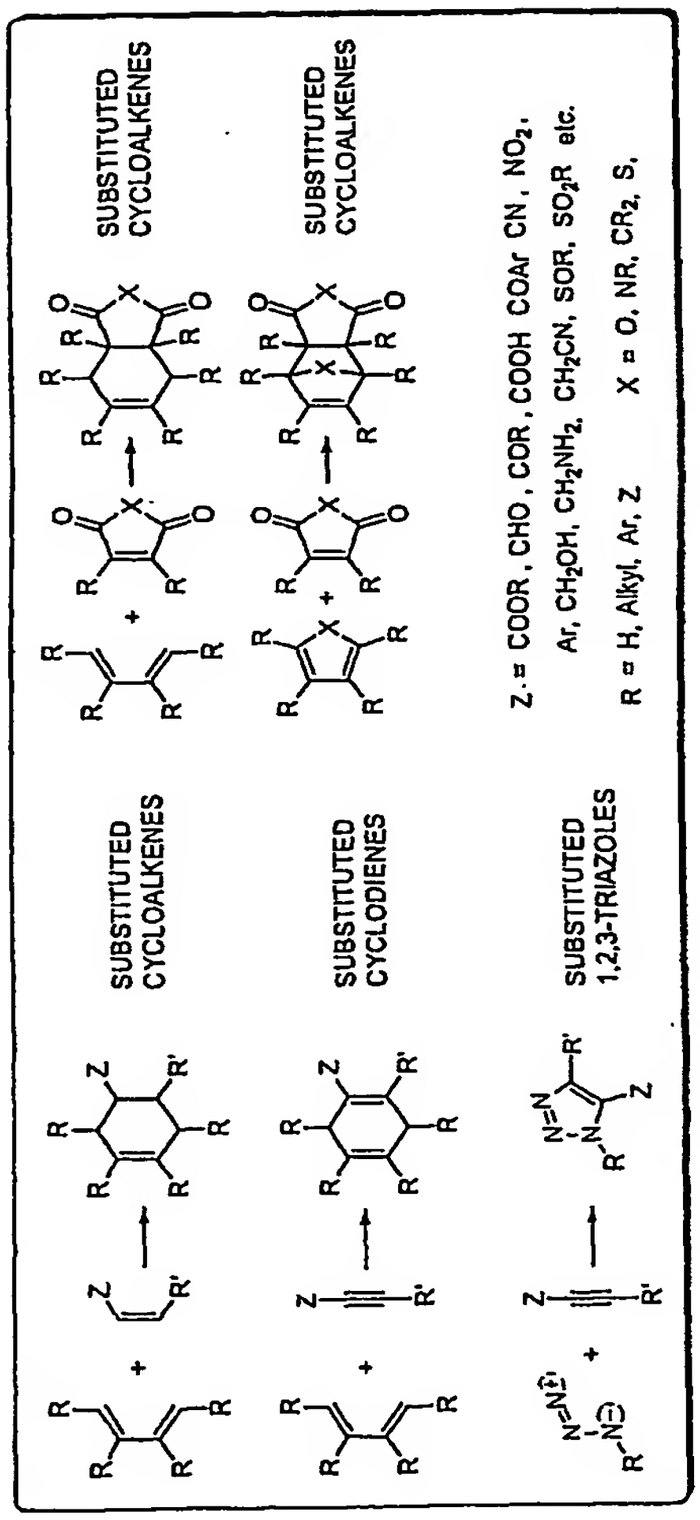
Figure 7. Pairs of reactive groups X,Y and the resulting bond XY.




Aromatic nucleophilic substitution
SUBSTITUTED AROMATIC COMPOUNDS
+ R'—Nu
Nu = Oxygen-, Nitrogen-, Sulfur- and Carbon Nucleophiles
X = F, Cl, Br, I, OSO_2CH_3, OSO_2CF_3, OSO_2TOL,., etc.
Z',Z = COOR, CHO, COR, $CONR'_2$, COO^-, CN,
NO_2, SOR, SO_2R, $SO_2NR'_2$,. ect.
Transition metal catalysed reactions
VINYL SUBSTITUTED AROMATIC COMPOUNDS
ALKYN SUBSTITUTED AROMATIC COMPOUNDS
BIARYL COMPOUNDS
+
Ar—X
$Pd(PPh_3)_4$


Addition to carbon-carbon multiplebonds
R'
R
+ R"—X
ETHERS
R"O
THIO-ETHERS
R"S
tert-AMINES
R"HN
sec-AMINES
R"N
R'''
HYDRA-ZINES
HNR"
HN
HYDROXYLAMINE ETHERS
OR"
HN
MULTI FUNCTIONAL COMPOUNDS
Z = H, Alkyl, Z', Ar
Z" = COOR, CHO, COR, CONR"2, CN, NO2, SOR, SO2R, SO2NR"2,.. ect.
Z' = Z" R = R', = R", = Z
DI- AND TRI-FUNCTIONAL ALKENES
Z = H, Alkyl, Ar,
Z" = Z', Alkyl, Ar,
Z' = COOR, CHO, COR, CONR"2, CN, NO2, SOR,
SO2R, SO2NR"2, ect.

Cycloadditions to multiple bounds



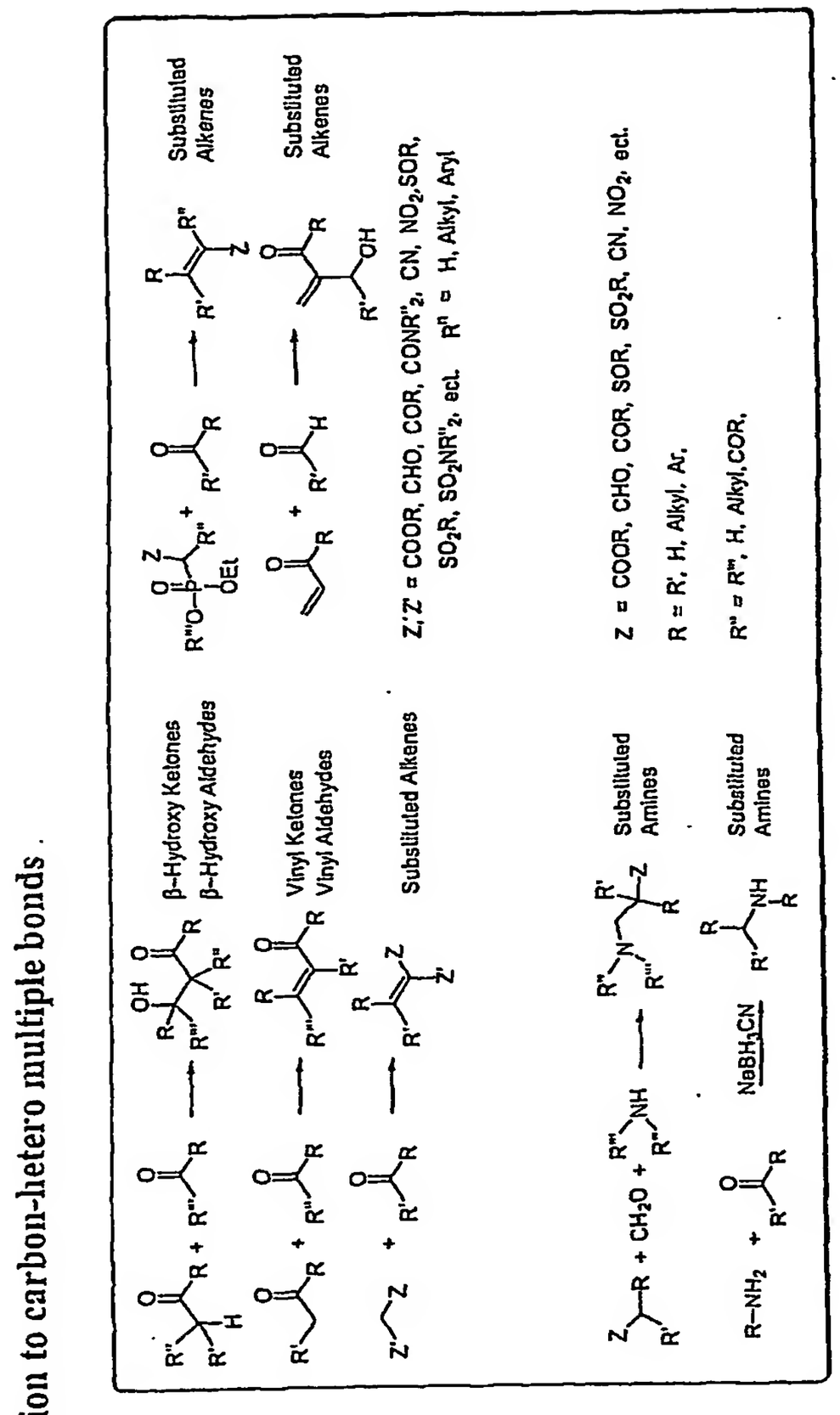
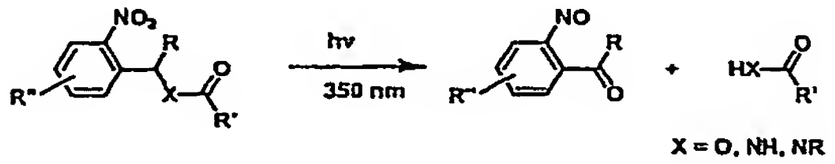
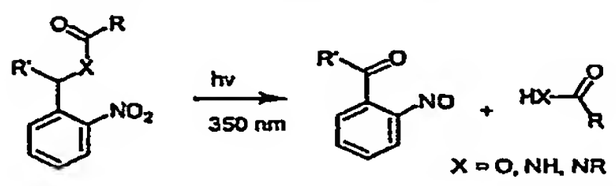

Addition to carbon-hetero multiple bonds
β-Hydroxy Ketones
β-Hydroxy Aldehydes
Substituted Alkenes
Vinyl Ketones
Vinyl Aldehydes
Substituted Alkenes
Substituted Alkanes
Substituted Amines
Substituted Amines
Z,Z' = COOR, CHO, COR, CONR"2, CN, NO2,SOR, SO2R, SO2NR"2, ect. R" = H, Alkyl, Ar,
Z = COOR, CHO, COR, SOR, SO2R, CN, NO2, ect.
R = R', H, Alkyl, Ar,
R" = R"', H, Alkyl,COR,

Figure 8. Cleavable Linkers

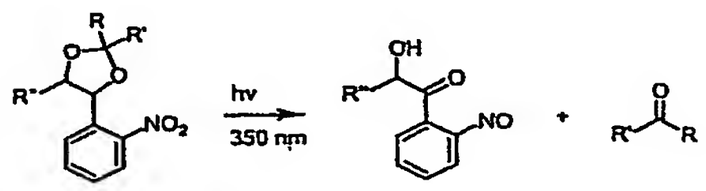
A. Linker for the formation of Ketones, Aldehydes, Amides and Acids



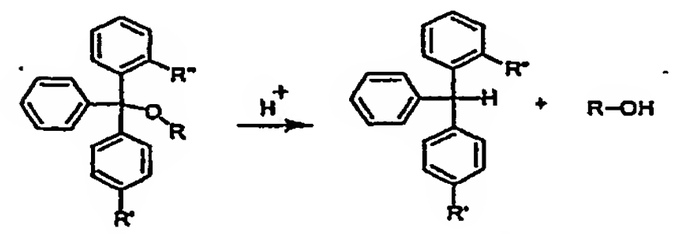
B. Linker for the formation of Ketones, Amides and Acids



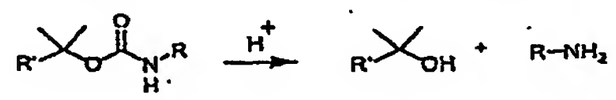
C. Linker for the formation of Aldehydes and Ketones



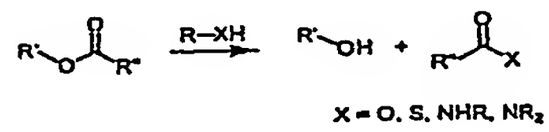
D. Linker for the formation of Alcohols and Acids



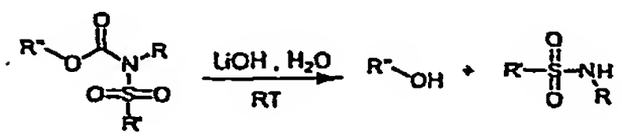
E. Linker for the formation of Amines and Alcohols



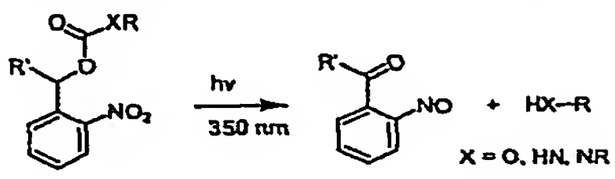
F. Linker for the formation of Esters, Thioesters , Amides and Alcohols



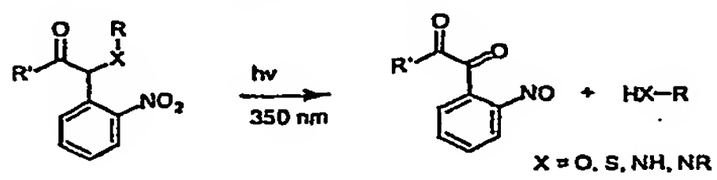
G. Linker for the formation of Sulfonamides and Alcohols



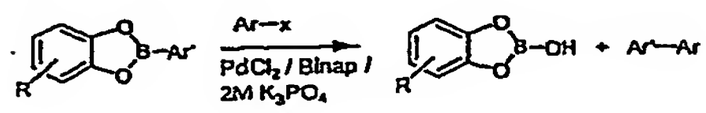
H. Linker for the formation of Ketones, Amines and Alcohols



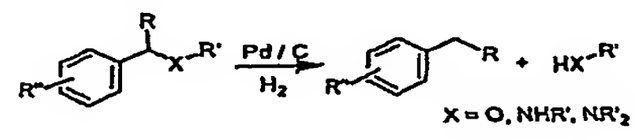
I. Linker for the formation of Ketones, Amines, Alcohols and Mercaptanes



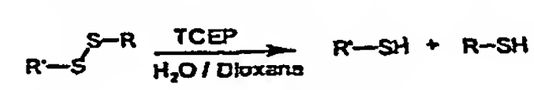
J. Linker for the formation of Biaryl and Bihetaryl



K. Linker for the formation of Benzyles, Amines, Anilins Alcohols and Phenoles



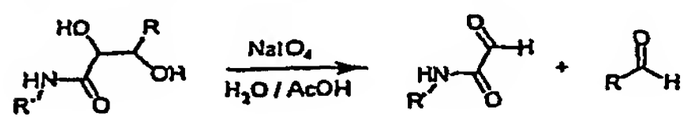
L. Linker for the formation of Mercaptanes



TCEP = tris(2-carboxyethyl)phosphine

M. Linker for the formation of Glycosides

N. Linker for the formation of Aldehydes and Glyoxylamides



O. Linker for the formation of Aldehydes, Ketones and Aminoalcohols